CLAIMS

1. The use of a protein isoprenylation inhibitor or of a pharmaceutically acceptable salt, solvate or derivative thereof for the manufacture of a medicament for the treatment of a HIV infection, a retroviral infection genetically related to HIV, or AIDS.

2. Use according to claim 1, wherein the protein isoprenylation inhibitor is an inhibitor of geranyl geranyl pyrophosphate synthase.

3. Use according to claim 1, wherein the protein isoprenylation inhibitor is an inhibitor of geranyl geranyl transferase.

4. Use according to claim 1, wherein the protein isoprenylation inhibitor is an inhibitor of Rho activation.

5. Use according to any one of claims 1 to 4, wherein the inhibitor is a statin or an analogue thereof.

6. Use according to claim 5, wherein the statin is selected from the group comprising lovastatin, simvastatin, pravastatin, mevastatin, atorvastatin and fluvastatin.

7. Use according to any one of claims 1 to 6, wherein in the protein isoprenylation inhibitor is admixed with a pharmaceutically acceptable carrier, binder, filler, vehicle, diluent, or excipient or any combination thereof.

8. Use according to any one of claims 1 to 7, wherein the protein isoprenylation inhibitor is administered in combination with one or more other therapeutic agent selected from the group comprising an HIV protease inhibitor, a non-nucleoside reverse transcriptase inhibitor, a nucleoside/nucleotide reverse transcriptase inhibitor, a CCR5 antagonist, an integrase inhibitor, an RNaseH inhibitor, a raft domain inhibitory agent, a cholesterol reducing agent, a protein prenylation reducing agent, a Rho-A GTPase inhibitor, and a glycosphingolipid reducing agent.

9. Use according to claim 8, wherein said glycosphingolipid reducing agent is a compound selected from the group consisting of:

D-t-3',4'-ethylenedioxy-1-phenyl-2-palmitoylamino-3-pyrrolidino-1-propanol,
D-t-4'-hydroxy-1-phenyl-2-palmitoylamino-3-pyrrolidino-1-propanol,
1-phenyl-2-palmitoylamino-3-pyrrolidino-1-propanol,
pharmaceutically acceptable salts thereof, and mixtures thereof.

10. Use according to claim 8 or 9, wherein said raft domain inhibitory agent dissociates raft domains.

11. Use according to claim 8 or 9, wherein said raft domain inhibitory agent inhibits the formation of raft domains.

12. Use according to any one of claims 8 to 11, wherein said chemokine receptor modulatory agent inhibits the formation of and/or dissociates membrane raft domains.

13. Use according to any one of claims 8 to 11, wherein said Rho-A GTPase inhibitor is a statin.

14. Use according to any one of claims 8 to 13, wherein the combination comprises separate, sequential or simultaneous administration of one or more of the agents.

15. Use according to any one of claims 8 to 14, wherein in the one or more agents is admixed with a pharmaceutically acceptable carrier, binder, filler, vehicle, diluent, or excipient or any combination thereof.

16. A protein isoprenylation inhibitor or a pharmaceutically acceptable salt, solvate or derivative thereof for use in the treatment of a HIV, a retroviral infection genetically related to HIV, or AIDS.

17. A method of treatment of a mammal suffering from HIV, a retroviral infection genetically related to HIV, or AIDS which comprises treating said mammal with a

therapeutically effective amount of one or more agents capable of inhibiting protein isoprenylation, or a pharmaceutically acceptable salt, solvate or derivative thereof.

18. The method of claim 9 further comprising administering to the patient a pharmaceutically effective amount of at least one agent selected from the group consisting of an antiviral agent, a chemokine receptor modulatory agent, a raft domain inhibitory agent, a cholesterol reducing agent, a protein prenylation reducing agent, a Rho-A GTPase inhibitor, and a glycosphingolipid reducing agent.

19. The method of claim 17 or claim 18, wherein in the one or more agents is admixed with a pharmaceutically acceptable carrier, binder, filler, vehicle, diluent, or excipient or any combination thereof.

20. The method of any one of claims 17 to 19, wherein said antiviral agent is an addition salt selected from the group consisting of an acid addition salt, a metal addition salt, an ammonium salt, and a salt formed with an organic base.

21. The method according to any one of claims 17 to 20, wherein said glycosphingolipid reducing agent is a compound selected from the group consisting of:

D-t-3',4'-ethylenedioxy-1-phenyl-2-palmitoylamino-3-pyrrolidino-1-propanol,
D-t-4'-hydroxy-1-phenyl-2-palmitoylamino-3-pyrrolidino-1-propanol,
1-phenyl-2-palmitoylamino-3-pyrrolidino-1-propanol,
pharmaceutically acceptable salts thereof, and mixtures thereof.

22. The method according to any one of claims 17 to 21, wherein said antiviral agent is a compound selected from the group consisting of nucleosides, nucleotides, protease inhibitors, pyrimidinones, and pyridinones.

23. The method according to any one of claims 17 to 22, wherein said raft domain inhibitory agent dissociates raft domains.

24. The method according to any one of claims 17 to 22, wherein said raft domain inhibitory agent inhibits the formation of raft domains.

25. The method according to any one of claims 17 to 24, wherein said chemokine receptor modulatory agent inhibits the formation of and/or dissociates membrane raft domains.

26. The method according to any one of claims 17 to 25, wherein said Rho-A GTPase inhibitor is a statin.

27. The method according to any one of claims 17 to 26, wherein the method further comprises separate, sequential or simultaneous administration of one or more of the agents.

28. A method of treatment of a mammal suffering from HIV, a retroviral infection genetically related to HIV, or AIDS by preventing the accumulation of HIV receptors in raft domains comprising providing a non-raft targeted mutant cytokine receptor.

29. The method according to Claim 28, wherein said mutant receptor binds HIV but does not enter into raft domains.

Abstract

The present invention relates generally to the prevention or delaying of retroviral infection by use of agents that prevent the clustering of retroviral receptors associated with cell membrane raft domains. The present invention relates more specifically to the prevention or treatment of HIV-1 infection through the use of agents that inhibit Rho-A activation by affecting GTPase activity or protein isoprenylation. The present invention relates also to the prevention or delay of HIV-1 infection through the displacement of cytokine receptors from cell membrane raft domains.

Table I. Clinical parameters of HIV-1-infected, statin-treated patients

Patient ID		#1	#2	#3	#4	#5	#6
Sex		Male	Male	Female	Male	Male	Male
Age		53	23	33	24	42	39
Virus transmission		Sexual	Sexual	IVDU[1]	Sexual	IVDU	IVDU
Diagnosis date		1997	2000	1996	ND	1998	1996
HAART		No	No	No	No	No	No
HCV[2] co-infection		No	No	Yes	No	Yes	Yes
Other		Ethylism, pancreatitis	Asthma	Methadone treatment	No	Methadone treatment	Methadone treatment
Viral load[3]	before	16,800	19,500	50,100	84,000	37,300	46,400
	after	2,330	9,940	12,138	3,590	21,600	26,300
	rebound[4]	16,100	56,100	64,000	26,400	26,400	32,600
$CD4^+$ (count/ml)	before	798	520	513	760	465	538
	after	940	560	540	1,010	487	552
	rebound	690	550	501	501	478	560

[1] Intravenous drug use. [2] Hepatitis C virus. [3] Viral load is expressed as HIV-1 RNA copies/ml,

[4] Measurements after three months without treatment.